

REMARKS

I. Amendments to the Claims:

Claim 82 is pending in the instant application.

Claim 82 has been amended and new claims 93-107 have been added herein. Support for the amendment to claim 82 and for the new claims can be found throughout the application as filed. For example, support can be found at page 48, line 23, to page 49, line 22; page 49, lines 31-36; page 50, lines 10-22; page 57, lines 4-9; and page 62, lines 15-20. Thus, no new matter has been added by way of the instant amendment.

Upon entry of the instant amendment, claims 82 and 93-107 will be pending in this application.

II. Withdrawal of Prior Rejection:

Applicants gratefully acknowledge that the Examiner has withdrawn the prior rejection of claim 82 under 35 U.S.C. § 103(a) as being unpatentable over Kagan (U.S. Patent No. 3,389,051) in view of Szycher *et al.* (CA117:239546).

III. Rejection under 35 U.S.C. § 103(a):

Claim 82 stands rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kagan (U.S. Patent No. 3,389,051) in view of Perricone (U.S. Patent No. 5,409,693) (*see*, Office Action, page 3).

As a preliminary matter, Applicants note that the Office Action includes Szycher in the arguments for nonpatentability of Applicants' claimed invention (*see*, Office Action, page 3, third full paragraph). However, as noted above, the Examiner has withdrawn the rejection based on Szycher (*see*, Office action, page 2, fifth full paragraph). Furthermore, Szycher is not included in the statement of the instant § 103 rejection (*see*, Office Action, page 3, first full paragraph). Accordingly, Applicants have not addressed the Office Action's arguments relating to Szycher below.

Applicants' amended claim 82 recites the following:

A pharmaceutical composition for reducing skin pigmentation, wherein the pharmaceutical composition is an ointment, cream, lotion or emulsion *formulated for percutaneous absorption* by topical administration, comprising a skin pigmentation reducing effective amount of a compound *and a dermatologically-acceptable carrier*, wherein the compound is selected from the group consisting of: [chemical structures II-VIII] and combinations thereof. (emphasis added).

Kagan discloses methods for reducing cholesterol in the body by administering particular chemical compounds, which include Applicants' compound VIII, that partially arrest the biosynthesis of cholesterol in the body (*see*, col. 1, ll. 1-20; and col. 2, ll. 36-40 of U.S. Patent No. 3,389,051). The disclosure of Kagan is focused on compositions for oral administration or injection for reducing cholesterol levels. This reference does not teach or suggest *topical* administration of the specific ointment-, cream-, lotion-, or emulsion-based cholesterol-lowering compositions formulated for any purpose, let alone for percutaneous absorption for reduction of skin pigmentation (*see, e.g.*, col. 4, lines 69-75; col. 5, lines 61-66; Examples 1-8; and claims 1-2 of U.S. Patent No. 3,389,051).

Perricone discloses methods for treatment of skin disorders caused by collagen deficiency, and/or oxygen-containing free radicals, and/or by oxidative generation of biologically-active metabolites, by topical administration of a fatty acid ester of ascorbic acid and a dermatologically-acceptable carrier (*see*, Abstract; and col. 2, ll. 26-38). Perricone does not teach or suggest administration of any of the specific compounds recited in claim 82 for *any* purpose, let alone for reducing skin pigmentation.

To support a *prima facie* case of obviousness, the cited references must teach or suggest every element of the claimed invention, and there must be some suggestion or motivation to combine the teachings of the cited references. The motivation to combine must be found in the prior art, and must not be based on impermissible hindsight in view of Applicants' disclosure. *See, e.g., In re Kotzab*, 217 F.3d 1365, 1369-1370 (Fed. Cir. 2000). Furthermore, the showing of

motivation to combine must be clear and particular, based on actual evidence, and not merely broad conclusory statements regarding the teachings of multiple references. *Id.* at 1370-1371.

Amended claim 82 is not *prima facie* obvious over Kagan and Perricone, either alone or in combination, because neither of the cited references provide any teaching nor suggestion regarding a pharmaceutical composition for reducing skin pigmentation formulated for percutaneous absorption by topical administration with a compound recited in claim 82 and a dermatologically-acceptable carrier.

The Office Action of May 18, 2006, states that Kagan discloses a compound corresponding to compound VIII of Applicants' claim 82, and that it would have been obvious to deliver this compound for percutaneous absorption in a cream or lotion in view of Perricone. The Office Action states that:

[t]he skilled artisan would have been motivated to make the composition in the form of a cream or lotion, and would have had a reasonable expectation of success, because creams and lotions are known dermatologically acceptable forms for percutaneous absorption (*see*, Office Action, paragraph bridging pages 3-4).

However, this statement for the motivation to combine Kagan and Perricone is wholly insufficient because it is merely conclusory. There is simply no reasoning provided by the Office Action for why the skilled artisan, at the time of the instant application, would combine teachings related to lowering cholesterol levels in the body (Kagan) with teachings to treat or prevent sunburns (Perricone). Thus, there is no motivation provided for why the ordinary skilled artisan would formulate compounds described by Kagan that are purportedly useful for lowering cholesterol levels in the body in the form of creams and lotions.

The Federal Circuit has noted that most inventions arise from a combination of old elements, and each element may often be found in the prior art. However, *mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole*. Rather, to establish a *prima facie* case of obviousness based on a combination of elements disclosed in the prior art, the [Office Action] must articulate the basis on which it concludes that it would have been obvious to make the claimed invention. *In re Kahn*, No. 04-1616 (Fed. Cir. March 22, 2006) (emphasis added). When the [Office Action] does not explain the motivation,

suggestion, or teaching that would have led the skilled artisan at the time of the invention to the claimed invention as a whole, we infer that the [Examiner] used hindsight to conclude that the invention was obvious. The "motivation-suggestion-teaching" requirement protects against the entry of hindsight into the obviousness analysis, a problem § 103 was meant to confront.

Id at 12.

In the instant case, the Examiner has not met the burden of articulating a clear and particular showing for why one of ordinary skill in the art would be motivated to combine compounds useful for lowering cholesterol with dermatologically-acceptable carriers to produce a pharmaceutical composition to reduce skin pigmentation. That creams and lotions are known to be dermatologically-acceptable forms for percutaneous absorption, as stated by the Office Action, is not a sufficient motivation to combine Kagan and Perricone. It appears that the Office Action has relied on impermissible hindsight reasoning using Applicants' disclosure as a blueprint to reconstruct Applicants' claimed invention from the cited references. Thus, in the absence of a proper motivation to combine Kagan with Perricone, a *prima facie* case of obviousness has not been established by the Office Action.

Furthermore, Applicants note that the Federal Circuit has announced that "[i]n order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicants' endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). It is unclear to Applicants why the Perricone reference would logically have commended itself to an inventor's attention in considering the problem addressed by the Kagan reference. More specifically, Applicants question why a person of ordinary skill in the art trying to reduce cholesterol levels in the body would look to art dealing with reduction of treating or preventing sunburns. Since the subject matter disclosed in Perricone is not relevant to the problem addressed in Kagan, Applicants respectfully aver that this rejection constitutes improper combination of references in non-analogous arts.

In sum, the Office Action has not established a case of *prima facie* obviousness. Accordingly, claim 82 is not obvious in view of the cited references alone or in combination.

Applicants respectfully request that the present rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Dependent claims 93-107 are also nonobvious over the cited art as they include all the limitations of independent claim 82. Furthermore, these dependent claims include limitations that are not taught by the cited references, either alone or in combination. Thus, dependent claims 93-107, like independent claim 82, are both novel and non-obvious.

IV. Rejection under 35 U.S.C. § 112, Second Paragraph:

Claim 82 is rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for recitation of the “effects an alteration in late endosomal/lysosomal trafficking” (*see*, Office Action, page 5).

Without acquiescing to this rejection, and purely with a view to expedite prosecution, Applicants have amended claim 82 to delete the phrase at issue. Accordingly, this rejection under 35 U.S.C. § 112, second paragraph, has been rendered moot.

V. Rejections under 35 U.S.C. § 112, First Paragraph, Enablement:

(a) Claim 82 stands rejected under 35 U.S.C. § 112, first paragraph, for purportedly lacking enablement (*see*, Office Action, page 6). Specifically, the Office Action alleges that the specification does not teach how to make the compounds of Formulas II-VIII.

Applicants traverse this rejection.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). Importantly, the Federal Circuit has held that a patent specification need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

Applicants direct the Examiner’s attention to **Appendix A** which is attached with this Response that provides evidence of references well before the priority date of the instant

application that teach how to make the compounds of Formulas II-VIII. Appendix A clearly evidences that it would not constitute undue experimentation to practice Applicants' claimed invention because one of ordinary skill in the art could follow the guidance in the cited references to make the compounds recited in Applicants' claims.

Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 112, first paragraph, enablement, be reconsidered and withdrawn.

(b) Claim 82 stands rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement (*see*, Office Action, page 7). Specifically, the Examiner purports that the specification lacks enablement of "altering late endosomal/lysosomal trafficking."

Without acquiescing to this rejection, and purely with a view to expedite prosecution, Applicants have amended claim 82 to delete the phrase at issue. Accordingly, the grounds for this rejection under 35 U.S.C. § 112, first paragraph, enablement, have been rendered moot.

CONCLUSION

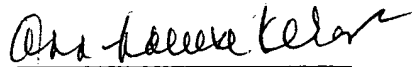
In view of the amendment and arguments set forth above, Applicants respectfully submit that the rejections in the Office Action mailed on May 18, 2006, have been overcome and that pending claims 82 and 93-107 are in condition for allowance.

Applicants petition for a three-month extension of time to respond to the outstanding Office Action. Please charge the requisite fees to our Deposit Account No. 08-0219. No other fees are due in connection with this correspondence; however, if any fees are due, please charge such fees or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is encouraged to telephone the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,

Dated: November 17, 2006



Ann-Louise Kerner, Ph.D.
Reg. No. 33,523

WILMER CUTLER PICKERING HALE AND DORR LLP

60 State Street
Boston, MA 02109
Tel: 617-526-6192
Fax: 617-526-5000